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REMARKS

The Applicants note the Examiner's objection to the word "know" in Claim 19, and now amend the word "know" to "known." Claims 1-27 are pending in the present case and stand rejected by the Examiner. The Claims stand rejected under 35 U.S.C. §112, 35 U.S.C. §102(b), and 35 U.S.C. §103(a). Claims 1, 18 and 19 are currently amended, and Claims 16 and 17 are cancelled. Each rejection is addressed below.

Applicants note that all amendments of Claims presented herein are made without acquiescing to any of the Examiner's arguments or rejections, and solely for the purpose of expediting the patent application process in a manner consistent with the PTO's Patent Business Goals (PBG),[1] and without waiving the right to prosecute the amended Claims (or similar Claims) in the future.

I. Claims 1-27 Are Rejected Under 35 U.S.C. § 112

The Examiner rejects Claims 1-27 under 35 U.S.C. § 112 "as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention." Office Action, pg. 2. In particular, the Examiner states "Claim 1 is vague and indefinite because it is not clear as to how the detectable signal is being detected at the reaction site." Office Action, pg. 2. The Applicant's respectfully disagree, however, to expedite prosecution, Claim 1 is now amended to explain that the assay test reaction site comprises a non-toxic chromogen. The Specification provides ample support for this amendment. (See, e.g., Specification, pg. 42). Claim 1 further specifies that the assay test reaction site is exposed in the mouth of a subject and contacted with oral fluid. The claim is therefore clear that the presence of the analyte in the oral fluid generates a detectable signal from the chromogen within the assay test reaction site. As amended, Claim 1 provides clear guidance as to how the detectable signal is detected at the reaction site. As such, the 35 U.S.C. §112 rejection should be withdrawn.

II. Vodian Does Not Anticipate Claims 1-2, 6 and 11

The Examiner rejects Claims 1-2, 6 and 11 under 35 U.S.C. § 102(b) as being anticipated by U.S. Patent No. 4,853,325 (hereinafter Vodian). The Applicants respectfully disagree with the Examiner's rejections. The Vodian reference is discussed in view of the amended claims. A claim is not anticipated by a prior art reference when that reference fails to describe each and

[1] 65 Fed. Reg. 54603 (Sept. 8, 2000).

every element as set forth in the contested claim. Verdegall Bros. v. Union Oil Co. of California, 814 F.2d 628 (Fed. Cir. 1987). Here, one element of Independent Claim 1 comprises exposing an assay test reaction site *inside* a subject's mouth. Vodian also describes an assay test with a reaction site, but, does not teach the exposure of the assay test reaction site to the inside of a subject's mouth. Column 5, Lines 15-18. In particular, Vodian states "the FeLV saliva test employs an immunological probe (2) for acquiring the saliva sample, for transferring the saliva sample to the incubation vessel (4), and for developing the color reactions." Column 5, Lines 15-18. As such, Vodian segregates the assay test reaction site from the inside of a subject's mouth with an incubation vessel. Vodian fails to meet each and every element contained in Claim 1, and therefore does not anticipate Claim 1. For the reasons discussed below, one would not want to expose the reaction site of Vodian inside a subject's mouth.

In addition, Vodian does not anticipate the use of an assay test reaction site comprising a non-toxic chromogen. Indeed, Vodian teaches a chromogenic substrate utilizing diethanolamine and 3,3',5,5'-tetramethylbenzidine (TMB). Vodian, Column 8, Lines 34-37, 55-59. Diethanolamine and TMB are toxic chemicals. See provided Medical Data Safety Sheets for each chemical. Diethanolamine and TMB are also irritants and/or carcinogenic; see Claims 18 and 19. Claim 1, as amended, provides an assay test reaction site comprising a non-toxic chromogen. Vodian does not teach of an assay test reaction site comprising a non-toxic chromogen, and therefore does not anticipate Claim 1. The Applicants request that this rejection be withdrawn.

III. Manautou Does Not Anticipate Claims 1-6, 11, and 16

The Examiner rejects Claims 1-6, 11, and 16 under 35 U.S.C. § 102(b) as being anticipated by U.S. Patent No. 3,875,013 (hereinafter Manatou et al). The Applicants respectfully disagree with the Examiner's rejections. As noted, a prior art reference does not anticipate a claim when it fails to meet each and every element of the claim. Verdegall Bros., 814 F.2d 628 (Fed. Cir. 1987). Manautou does not provide a reaction site that 1) produces a detectable signal in the presence of an analyte and 2) that is exposed inside a subject's mouth. Manautou discusses the use of test strips in characterizing a female subject's ovulation schedule. In one embodiment, Manautou provides touching a test strip onto a subject's tongue, *removing* the test strip from the subject's mouth, and adding reagents to develop the color. Manautou's reaction site never is exposed inside a subject's mouth when it is capable of producing a detectable signal. Furthermore, the p-nitrophenol of Manautou is *not* a non-toxic chromogen (see attachment). Column 3, Lines 30-58. As such, Manautou does not meet each and every

element of Claim 1, and therefore does not anticipate Claim 1. The Applicants request the rejection be withdrawn.

IV. Sangha Does Not Anticipate Claims 1-5, 8-12, and 16

The Examiner rejects Claims 1-5, 8-12, and 16 under 35 U.S.C. § 102(b) as being anticipated by U.S. Patent No. 5,334,502 (hereinafter Sangha). The Applicants respectfully disagree with the Examiner's rejections. As noted, a prior art reference does not anticipate a claim when it fails to meet each and every element of the claim. Verdegall Bros., 814 F.2d 628 (Fed. Cir. 1987). Here, one element of Independent Claim 1 comprises exposing an assay test reaction site inside a subject's mouth. Sangha pertains to a method of collecting, identifying, and quantifying saliva. However, Sangha fails to describe an embodiment where the assay test reaction site is directly exposed to the inside of a subject's mouth. See, e.g., Sangha, Column 5, Lines 44-54, Column 8, Lines 3-17, Column 8, Lines 37-52, Column 8, Lines 53-64. In each embodiment described by Sangha, the assay test reaction site is segregated from the inside of a subject's mouth. Sangha differs from Claim 1 in that it fails to teach of an assay test reaction site directly exposed to the inside of a subject's mouth. Furthermore, Sangha utilizes TMB which is *not* a non-toxic chromogen (see attachment). As such, Sangha does not meet each and every element of Claim 1, and does not anticipate Claim 1. The Applicants respectfully request this rejection be withdrawn.

V. Claims 6, 7, 13-15, 17-19, and 20-27 are Nonobvious

Claims 6, 7, 13-15, 17-19, and 20-27, stand rejected under 35 U.S.C. § 103(a) as allegedly being obvious in light of Sangha and U.S. Patent No. 6,248,598 (hereinafter Bogema), in light of Sangha and U.S. Patent No. 5,494,831 (hereinafter Kindler), and Sangha in light of U.S. Patent No. 4,562,043 (hereinafter Mennen). The Applicants respectfully disagree and assert that the Examiner does not present a prima facie showing of obviousness.

The present invention provides a test with an assay test reaction site that is exposed inside a subject's mouth and that can produce a detectable signal. This provides an improvement over the prior art – much of which requires complex multi-step tests where saliva is collected and then separately assayed for color. A limiting factor of the prior art is the fact that most chromogens in use are toxic if taken orally. Thus, the prior art tests are 1) not used orally and require multi-step detection; and/or 2) are dangerous. The present invention solves this problem. Nothing in any of the cited references teach or suggest tests with reaction sites that are non-toxic and that are used orally. Thus, the prior art does not teach or suggest the claim limitations of the amended Claim 1. An invention is nonobvious if the prior art does not teach or suggest all of the claim

limitations. MPEP § 2143.03; *In re* Royka, 490 F.2d 981 (CCPA 1974). In addition, all dependent claims of a nonobvious independent claim are nonobvious. *In re* Fine, 837 F.2d 1071 (Fed. Cir. 1988). Here, Claims 6, 7, 13-15, 17-19, and 20-27 are all dependent upon Independent Claim 1. Claim 1 provides an assay test reaction site that is exposed to the inside of a subject's mouth. For the reasons discussed above, the prior art of record fails to teach or suggest an assay test reaction site with a non-toxic chromogen that is directly exposed to the inside of a subject's mouth. As a result, the prior art fails to teach or suggest all of the claim limitations. Additionally, none of the references cited by the Examiner addressing elements found in the dependent claims compensate for the fact that the primary references, alone or in combination with the secondary references, do not teach or suggest all the elements of the independent claims. The present invention is therefore nonobvious, and the Applicants respectfully request the rejections be withdrawn.

CONCLUSION

All grounds of rejection of the Office Action of September 27, 2002 having been addressed, it is respectfully submitted that the invention as claimed fully meets all requirements and that the claims should be passed to allowance.

Dated: March 10, 2003

David A. Casimir
Registration No. 42,395

MEDLEN & CARROLL, LLP
101 Howard Street, Suite 350
San Francisco, California 94105
(608) 218-6900

Appendix I

Pending Claims

1. (AMENDED) A method for detecting the presence of an analyte in [saliva]oral fluid, comprising:
   a) providing an assay test comprising a reaction site that produces a detectable signal in presence of an analyte; wherein said reaction site comprises a non-toxic chromogen;
   b) placing said reaction site into a mouth of a subject under conditions such that [saliva]oral fluid from said subject is contacted with said reaction site; and
   c) detecting the presence or absence of said detectable signal in said reaction site.

18. (AMENDED) The method of Claim 1[6], wherein said chromogen is a non-irritant.

19. (AMENDED) The method of Claim 1[6], wherein said chromogen is not a known carcinogen.

Appendix II
Pending Claims

1. A method for detecting the presence of an analyte in oral fluid, comprising:
   a) providing an assay test comprising a reaction site that produces a detectable signal in presence of an analyte; wherein said reaction site comprises a non-toxic chromogen;
   b) placing said reaction site into a mouth of a subject under conditions such that oral fluid from said subject is contacted with said reaction site; and
   c) detecting the presence or absence of said detectable signal in said reaction site.

2. The method of Claim 1, wherein said detectable signal comprises a color change.

3. The method of Claim 1, said assay test comprises a test strip.

4. The method of Claim 3, wherein said test strip comprises an absorbent material, wherein said reaction site is located within said absorbent material.

5. The method of Claim 1, wherein said reaction site comprises an enzyme, wherein said analyte is a substrate for said enzyme.

6. The method of Claim 1, wherein said reaction site comprises an antibody, wherein said antibody binds to said analyte.

7. The method of Claim 1, wherein said reaction site comprises a biosensor.

8. The method of Claim 5, wherein said enzyme produces oxidation and reduction products when reacted with said analyte.

9. The method of Claim 8, wherein said reaction site further comprises a chromogen.

10. The method of Claim 8, wherein said chromogen undergoes a color change in the presence of said oxidation and reduction products.

11. The method of Claim 2, wherein said color change is detectable by the human eye.

12. The method of Claim 1, wherein in step b), said reaction site is held in said mouth for a sufficient amount of time to generate said detectable signal while said reaction site is in said mouth.

13. The method of Claim 1, wherein in step b), said reaction site is held in said mouth for a sufficient amount of time to generate a detectable signal faster than when said reaction site is held in said mouth for 5 seconds.

14. The method of Claim 1, wherein in step b), said reaction site is held in said mouth for 10 seconds or more.

15. The method of Claim 14, wherein in step b), said reaction site is held in said mouth for 30 seconds or more.

18. The method of Claim 1, wherein said chromogen is a non-irritant.

19. The method of Claim 1, wherein said chromogen is not a known carcinogen.

20. The method of Claim 1, wherein said analyte comprises an alcohol moiety.

21. The method of Claim 20, wherein said analyte comprises ethanol.

22. The method of Claim 20, wherein said analyte comprises glucose.

23. The method of Claim 1, wherein said analyte comprises a ketone moiety.

24. The method of Claim 23, wherein said analyte comprises a ketone body.

25. The method of Claim 1, wherein said analyte comprises prostate-specific antigen.

26. The method of Claim 1, wherein said analyte comprises melatonin.

27. The method of Claim 1, wherein said analyte comprises lactoferrin.

Safety data for 3,3',5,5'-tetramethylbenzidine

Synonyms: 1,1'-biphenyl-4,4'-diamine
Molecular formula: C16 H20 N2
CAS No: 54827177
EC No:

Physical data

Appearance: pale yellow crystals
Melting point: 168 C
Boiling point:
Vapour density:
Vapour pressure:
Specific gravity:
Flash point:
Explosion limits:
Autoignition temperature:

Stability

Stable. Incompatible with water. Moisture sensitive.

Toxicology

Harmful by ingestion, inhalation and skin contact. Skin and eye irritant. **Mutagen. Should be treated as a potential carcinogen.** R20 R21 R22get "

Personal protection

Safety glasses, rubber or plastic gloves. Good ventilation.

Safety data for diethanolamine

General

Synonyms: 2,2'-iminobisethanol, 2,2'-iminodiethanol, diethylolamine
Molecular formula: $(HOCH_2CH_2)_2NH$
CAS No: 111-42-2
EC No:

Physical data

Appearance: solid or viscous liquid with an amine odour
Melting point: 28 C
Boiling point: 268 C (decomposes)
Vapour density: 3.6 (air = 1)
Vapour pressure:
Density (g cm^{-3}): 1.09
Flash point: 169 C (closed cup)
Explosion limits:
Autoignition temperature:
Water solubility: miscible

Stability

Stable. Incompatible with carbon dioxide, strong acids, strong oxidizing agents. Deliquescent.

Toxicology

Harmful if swallowed or inhaled. Severe skin, eye and respiratory irritant. Typical TLV/TWA 3 ppm.

Toxicity data
(The meaning of any abbreviations which appear in this section is given here.)
ORL-RAT LD50 710 mg kg^{-1}
IPR-RAT LD50 2300 mg kg^{-1}
SCU-MUS LD50 3553 mg kg^{-1}

Risk phrases
(The meaning of any risk phrases which appear in this section is given here.)
R20 R21 R22 R36 R37 R38.

Transport information

Personal protection

Safety glasses, gloves, adequate ventilation.

Safety phrases
(The meaning of any safety phrases which appear in this section is given here.)

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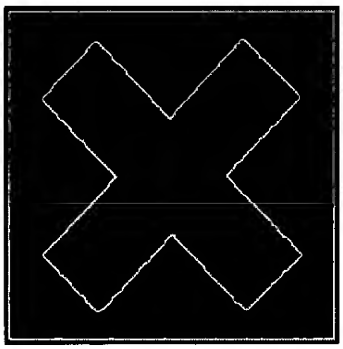
International Chemical Safety Cards

p-NITROPHENOL

ICSC: 0066

p-NITROPHENOL
4-Nitrophenol
4-Hydroxybenzene
$C_6H_5NO_3$
Molecular mass: 139.1
CAS # 100-02-7
RTECS # SM2275000
ICSC # 0066
UN # 1663
EC # 609-015-00-2



TYPES OF HAZARD/ EXPOSURE	ACUTE HAZARDS/ SYMPTOMS	PREVENTION	FIRST AID/ FIRE FIGHTING
FIRE	Combustible. Gives off irritating or toxic fumes (or gases) in a fire.	NO open flames.	Powder, water spray, foam, carbon dioxide.
EXPLOSION	Finely dispersed particles form explosive mixtures in air.	Prevent deposition of dust; closed system, dust explosion-proof electrical equipment and lighting.	In case of fire: keep drums, etc., cool by spraying with water.
EXPOSURE		PREVENT DISPERSION OF DUST! STRICT HYGIENE!	
INHALATION	Burning sensation. Cough. Dizziness. Weakness.	Local exhaust or breathing protection. Ventilation, local exhaust, or breathing protection.	Fresh air, rest. Refer for medical attention.
SKIN	MAY BE ABSORBED! (Further see Inhalation).	Protective gloves. Protective clothing.	Remove contaminated clothes. Rinse and then wash skin with water and soap. Refer for medical attention.
EYES	Redness. Pain.	Face shield or eye protection in combination with breathing protection.	First rinse with plenty of water for several minutes (remove contact lenses if easily possible), then take to a doctor.
INGESTION			